comprising epothilone B (where R = Me). Applicants thus respectfully submit that these claims are not duplicates and respectfully request that the Examiner withdraw the objection of claims 59 and 69.

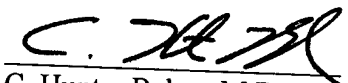
VI. Information Disclosure:

Applicants have provided herewith a modified PTO 1449 form citing a U.S. patent application (US 2002/0028839) published on March 7, 2002, entitled "Cancer Treatment with Epothilones". Applicants respectfully point out to the Examiner that the earliest priority date of this application (resulting from GB application number 9803907.6) is February 25, 1998, which date is *after* the actual filing date of Applicant's priority patent application (08/986,025, filed December 3, 1997, now U.S. Patent 6,242,469, the earliest priority date of which results from U.S. provisional application number 60/032,282, filed December 3, 1996).

REMARKS

If it is believed that a telephone conversation would expedite matters, the Examiner is invited to contact the undersigned at (617) 248-5215. The Examiner is authorized to charge any fees associated with this amendment, or to refund fees for any overpayment, to our Deposit Account No.: 03-1721

Respectfully submitted,



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Boston, MA 02109
(617) 248-5215 (Phone)
(617) 248-4000 (FAX)
Date: July 16, 2002

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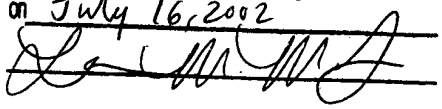
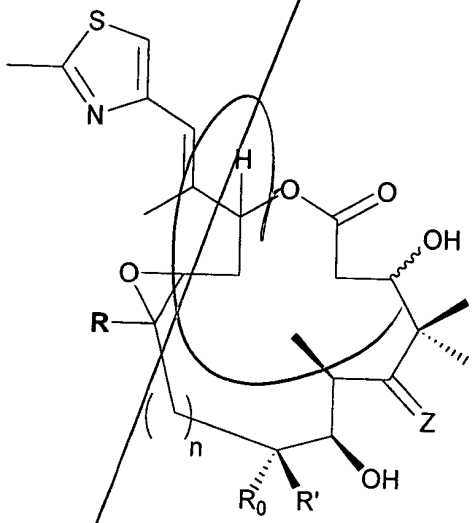
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, D.C. 20231
on July 16, 2002



Pending Claims (after entry of amendment)

30. A pharmaceutical composition for treating cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



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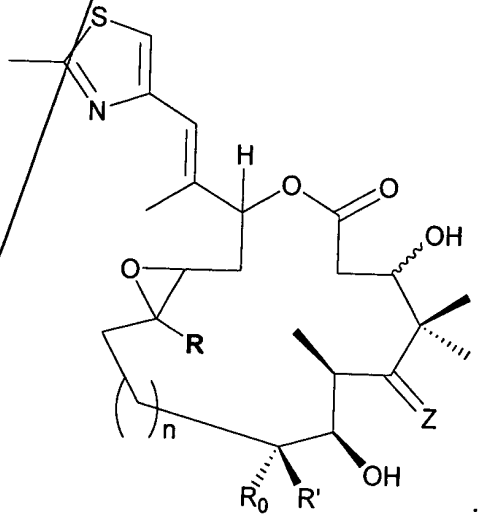
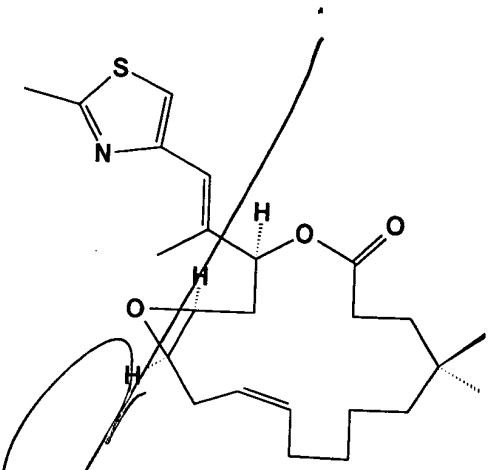
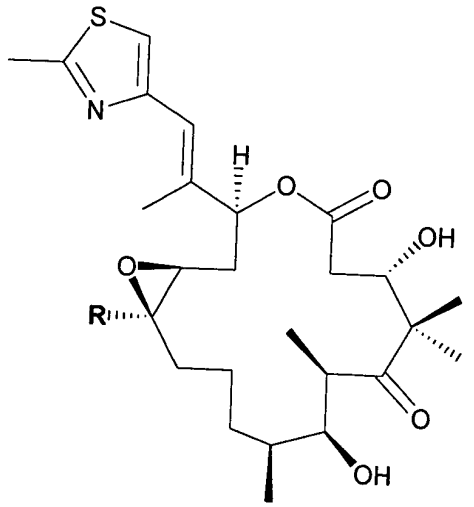


; or

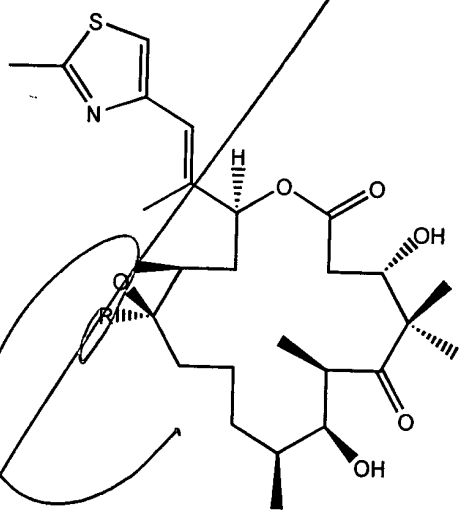


wherein R, R_0, and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

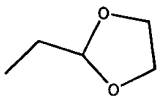
59. The pharmaceutical composition of claim 30, wherein the compound has the structure:



60. A pharmaceutical composition comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



wherein R is hydrogen, methyl, ethyl, n-propyl, n-butyl, n-hexyl, CH_2OH, $(CH_2)_3OH$, or



; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

61. The pharmaceutical composition of claim 60, wherein R is hydrogen.

62. The pharmaceutical composition of claim 60, wherein R is ethyl.

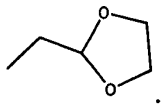
63. The pharmaceutical composition of claim 60, wherein R is propyl.

64. The pharmaceutical composition of claim 60, wherein R is n-butyl.

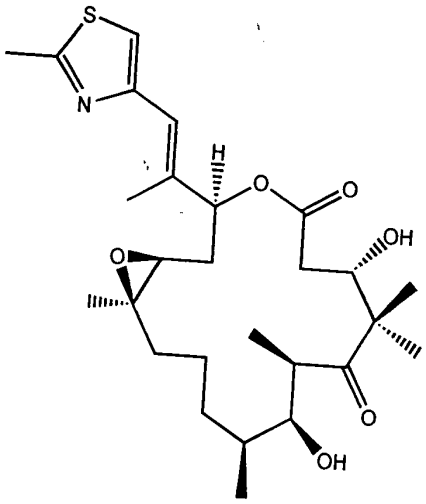
65. The pharmaceutical composition of claim 60, wherein R is n-hexyl.

66. The pharmaceutical composition of claim 60, wherein R is CH_2OH.

67. The pharmaceutical composition of claim 60, wherein R is $(CH_2)_3OH$.

68. The pharmaceutical composition of claim 60, wherein R is  .

69. A pharmaceutical composition comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



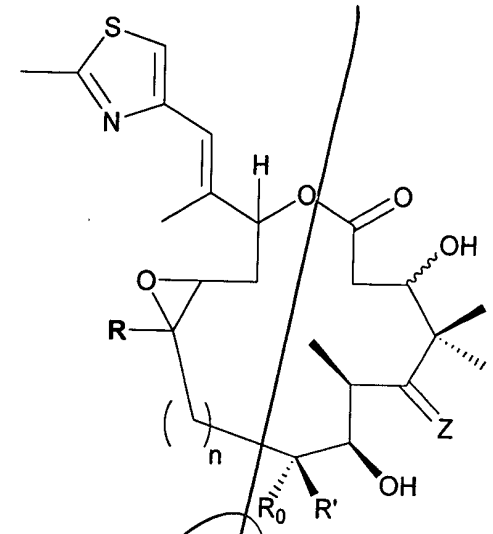
; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

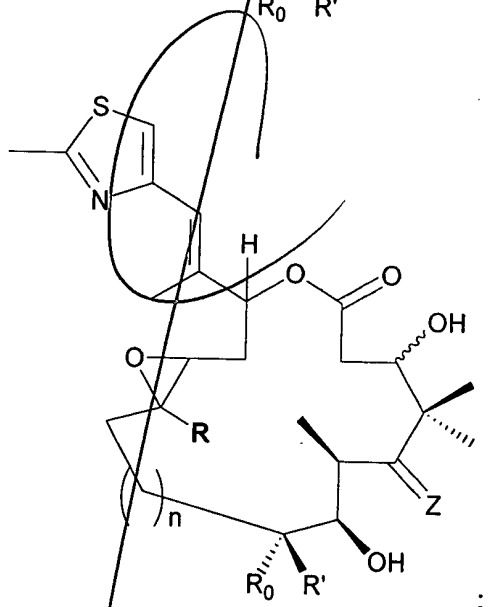
70. The pharmaceutical composition of claim 69, further comprising vinblastine.

71. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:

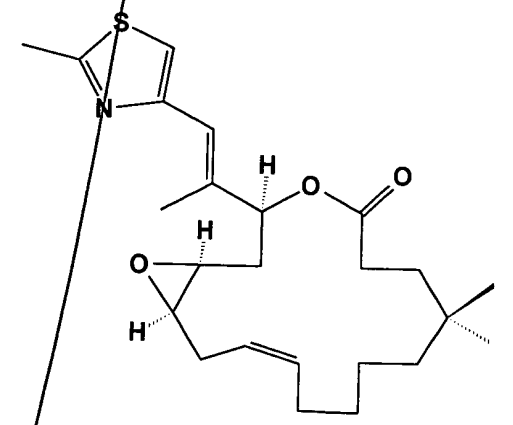
B32
cont



;



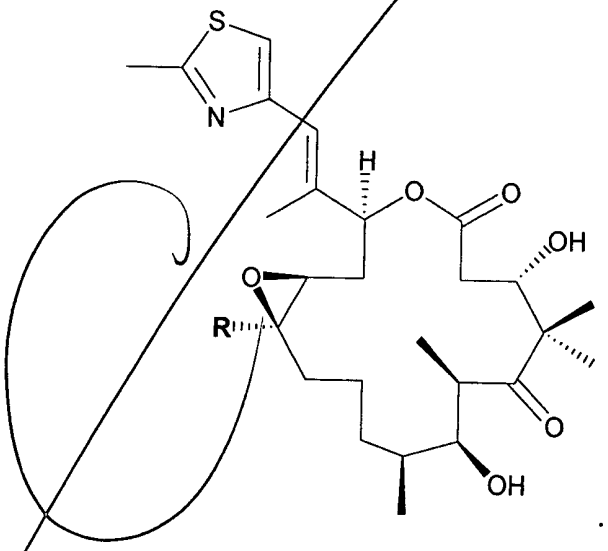
; or



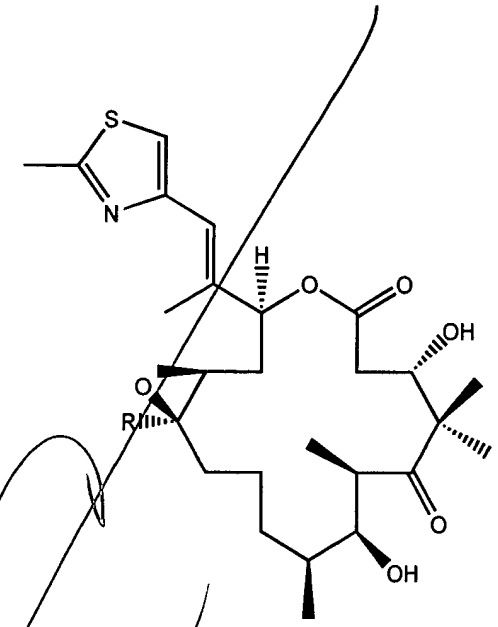
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally

substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

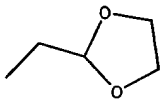
72. The method of claim 71, comprising administering a therapeutically effective amount of a compound having the structure:



73. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



wherein R is hydrogen, methyl, ethyl, n-propyl, n-butyl, n-hexyl, CH_2OH, $(CH_2)_3OH$, or



; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

74. The method of claim 73, wherein in the compound R is hydrogen.

75. The method of claim 73, wherein in the compound R is ethyl.

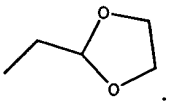
76. The method of claim 73, wherein in the compound R is propyl.

77. The method of claim 73, wherein in the compound R is n-butyl.

78. The method of claim 73, wherein in the compound R is n-hexyl.

79. The method of claim 73, wherein in the compound R is CH_2OH.

80. The method of claim 73, wherein in the compound R is $(CH_2)_3OH$.

81. The method of claim 73, wherein in the compound R is  .

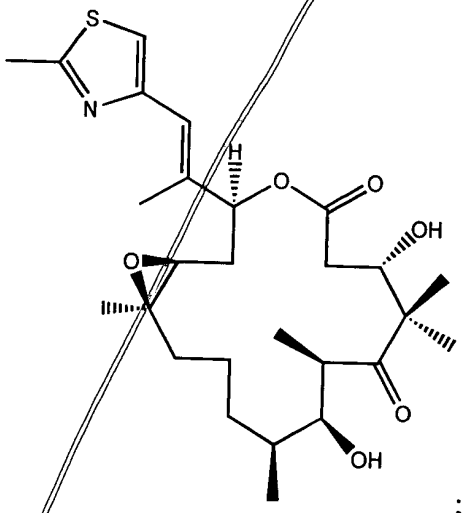
82. The method of claim 73, wherein the effective amount is between about 0.001 mg/kg and about 25 mg/kg.

83. The method of claim 73, wherein the cancer is a solid tumor.

84. The method of claim 73, wherein the cancer is breast cancer, melanoma, leukemia or ovarian cancer.

85. The method of claim 73, wherein the cancer is an MDR-resistant cancer.

86. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

87. The method of claim 86, wherein the effective amount is between about 0.001 mg/kg and about 1 mg/kg.

88. The method of claim 86, wherein the effective amount is between about 0.01 and 0.6 mg/kg.

89. The method of claim 86, wherein the effective amount is between about 0.01 mg/kg and about 0.3 mg/kg.

90. The method of claim 86, wherein the effective amount is between about 0.4 mg/kg and about 0.8 mg/kg.

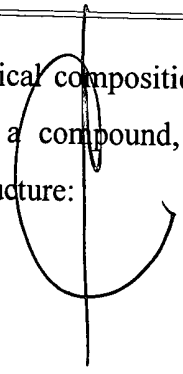
91. The method of claim 86, wherein the effective amount is between about 0.3 mg/kg and about 0.6 mg/kg.

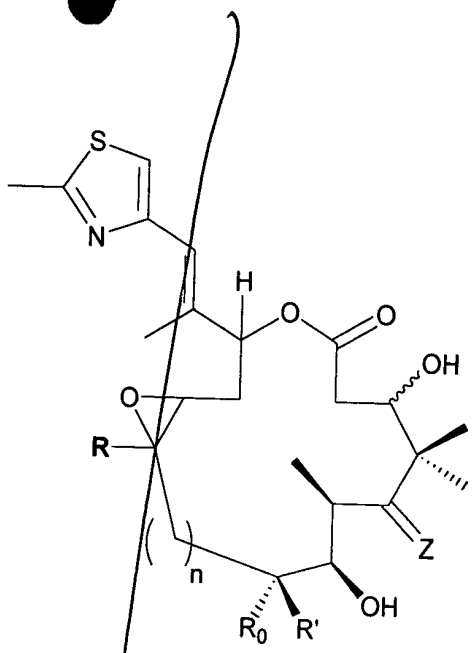
92. The method of claim 86, wherein the cancer is a solid tumor.

93. The method of claim 86, wherein the cancer is breast cancer, melanoma, leukemia or ovarian cancer.

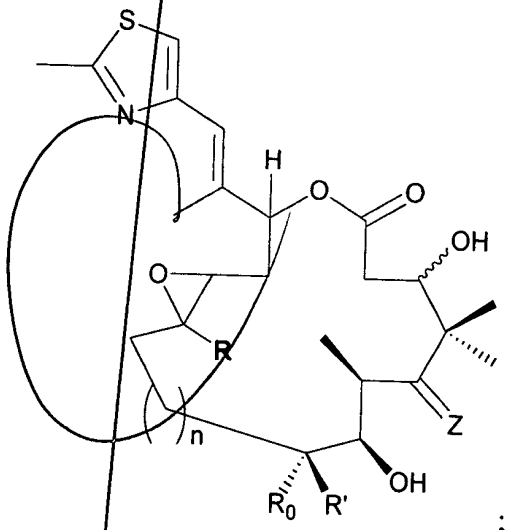
94. The method of claim 86, wherein the cancer is an MDR-resistant cancer.

95. A pharmaceutical composition for the treatment of cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:

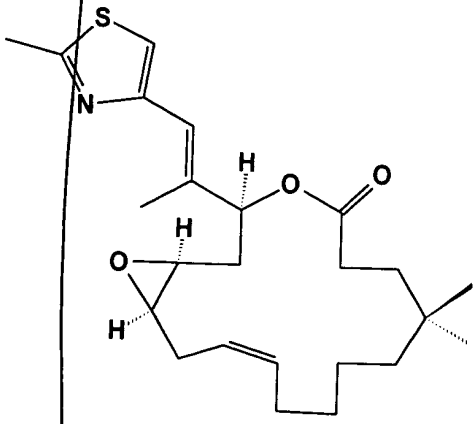




;



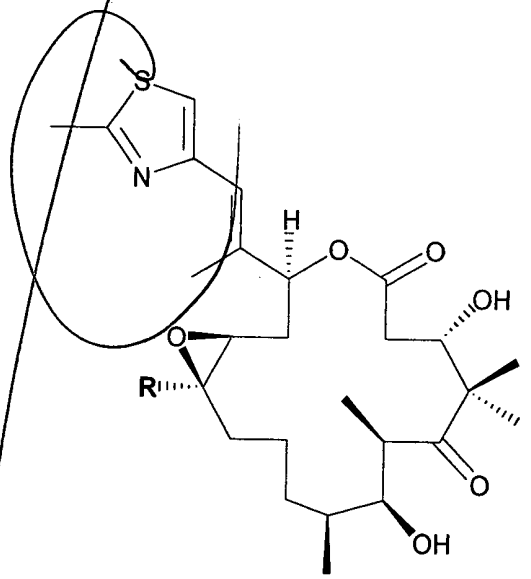
; or



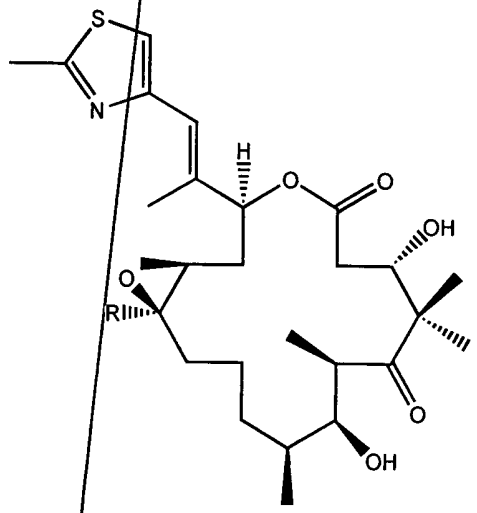
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally

substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3, and pharmaceutically acceptable salts thereof; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.01 mg to about 25 mg compound per kg body weight of a subject.

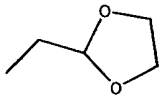
96. The pharmaceutical composition of claim 95, wherein the compound has the structure:



97. A pharmaceutical composition for the treatment of cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



wherein R is hydrogen, methyl, ethyl, n-propyl, n-butyl, n-hexyl, CH_2OH, $(CH_2)_3OH$, or



, and pharmaceutically acceptable salts thereof; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.01 mg to about 25 mg compound per body weight of a subject.

98. The pharmaceutical composition of claim 97, wherein R is hydrogen.

99. The pharmaceutical composition of claim 97, wherein R is ethyl.

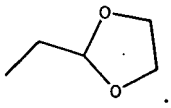
100. The pharmaceutical composition of claim 97, wherein R is propyl.

101. The pharmaceutical composition of claim 97, wherein R is n-butyl.

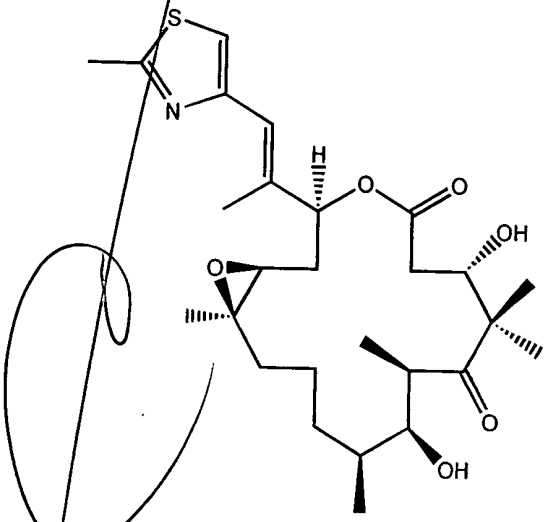
102. The pharmaceutical composition of claim 97, wherein R is n-hexyl.

103. The pharmaceutical composition of claim 97, wherein R is CH_2OH.

104. The pharmaceutical composition of claim 97, wherein R is $(CH_2)_3OH$.

105. The pharmaceutical composition of claim 97, wherein R is  .

106. A pharmaceutical composition for the treatment of cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



and pharmaceutically acceptable salts thereof; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.01 mg to about 25 mg compound per kg body weight of a subject.

107. The pharmaceutical composition of claim 106, further comprising vinblastine.

108. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.001 mg to about 1 mg compound per kg body weight.

109. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.01 mg to about 0.6 mg compound per kg body weight.

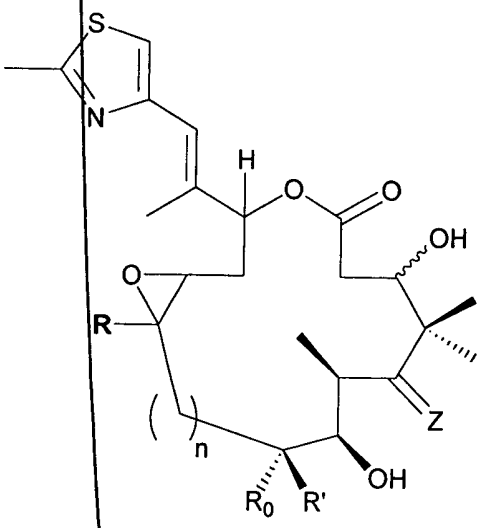
110. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.01 mg to about 0.3 mg compound per kg body weight.

111. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.4 mg to about 0.8 mg compound per kg body weight.

112. The pharmaceutical composition of claim 106, wherein the therapeutically effective amount is an amount sufficient to deliver about 0.3 mg to about 0.6 mg compound per kg body weight.

113. A method of treating cancer in a subject suffering therefrom comprising:

administering to the subject more than one dosage of a therapeutically effective amount of a compound having the structure:



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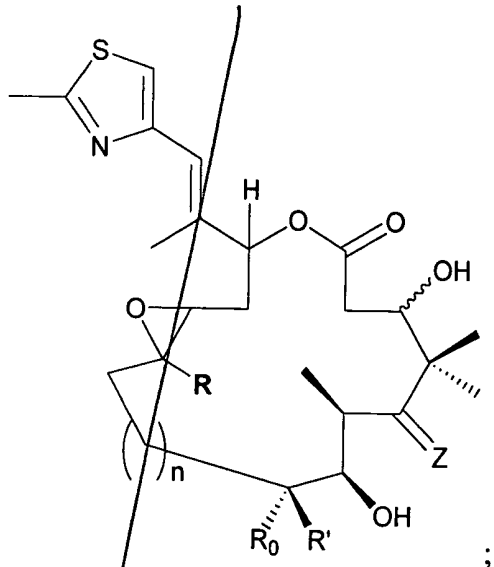
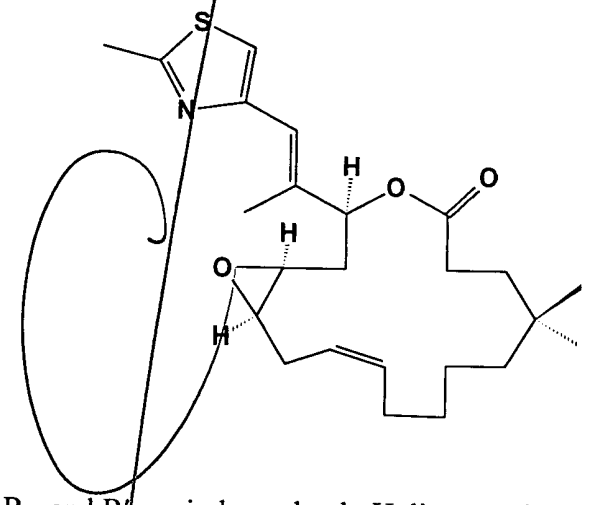


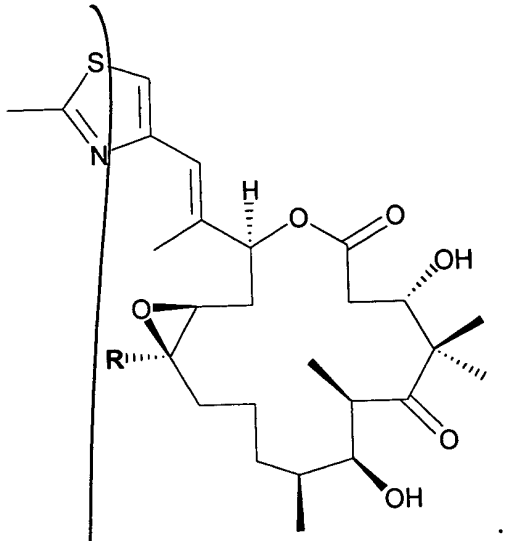
; or



wherein R, R_0, and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3, and pharmaceutically acceptable salts thereof;

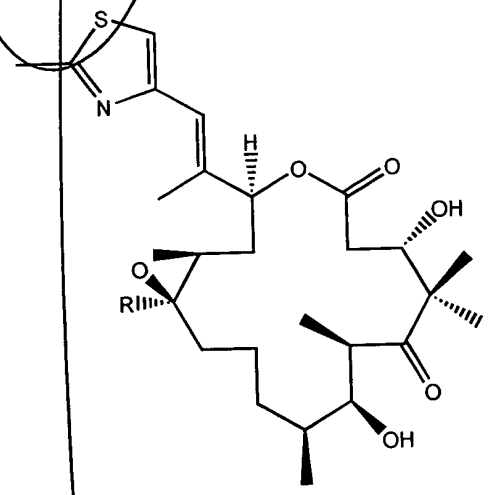
wherein each dosage administration comprises a therapeutically effective amount sufficient to deliver about 0.001 mg to about 25 mg compound per kg body weight.

114. The method of claim 113, wherein the compound administered has the structure:

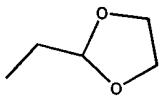


115. A method of treating cancer in a subject suffering therefrom comprising:

administering to the subject more than one dosage of a therapeutically effective amount of a compound having the structure:



wherein R is hydrogen, methyl, ethyl, n-propyl, n-butyl, n-hexyl, CH_2OH, $(CH_2)_3OH$, or



, and pharmaceutically acceptable salts thereof;

wherein each dosage administration comprises a therapeutically effective amount sufficient to deliver about 0.001 mg to about 25 mg compound per kg body weight.

116. The method of claim 115, wherein in the compound R is hydrogen.

117. The method of claim 115, wherein in the compound R is ethyl.

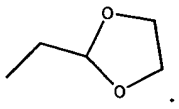
118. The method of claim 115, wherein in the compound R is propyl.

119. The method of claim 115, wherein in the compound R is n-butyl.

120. The method of claim 115, wherein in the compound R is n-hexyl.

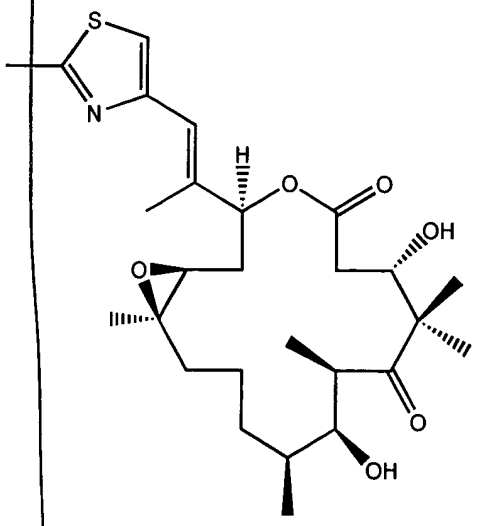
121. The method of claim 115, wherein in the compound R is CH_2OH.

122. The method of claim 115, wherein in the compound R is $(CH_2)_3OH$.

123. The method of claim 115, wherein in the compound R is  .

124. A method of treating cancer in a subject suffering therefrom comprising:

administering to the subject more than one dosage of a therapeutically effective amount of a compound having the structure:



wherein each dosage administration comprises a therapeutically effective amount sufficient to deliver about 0.001 mg to about 25 mg compound per kg body weight.

125. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.001 mg to about 1 mg compound per kg body weight.

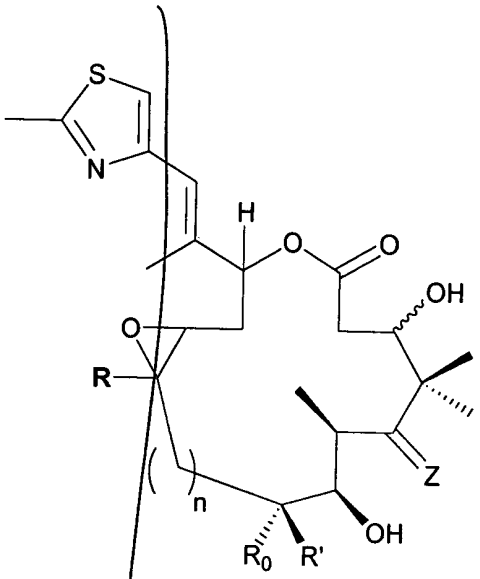
126. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.01 to about 0.6 mg compound per kg body weight.

127. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.01 mg to about 0.3 mg compound per kg body weight.

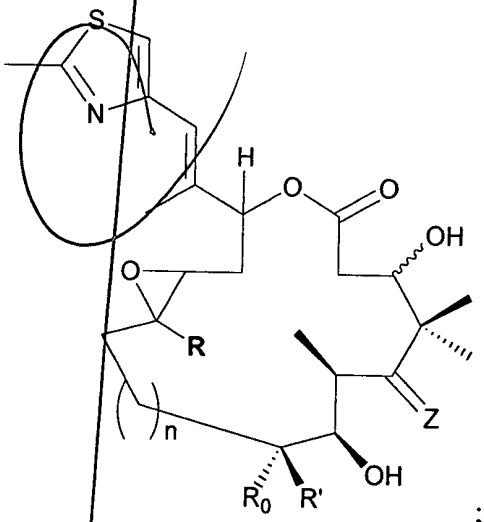
128. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.4 mg to about 0.8 mg compound per kg body weight.

129. The method of claim 124, wherein the therapeutically effective amount of each dosage administration is an amount sufficient to deliver about 0.3 mg to about 0.6 mg compound per kg body weight.

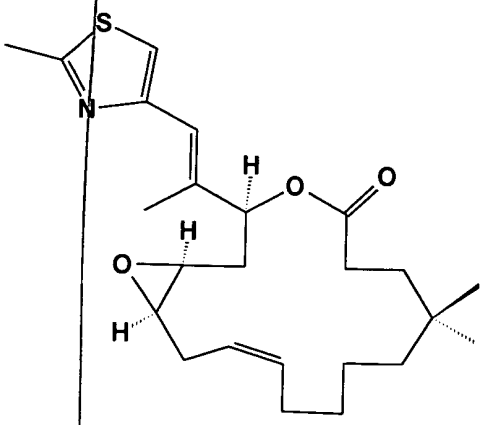
130. A pharmaceutical composition for treating cancer comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:



;



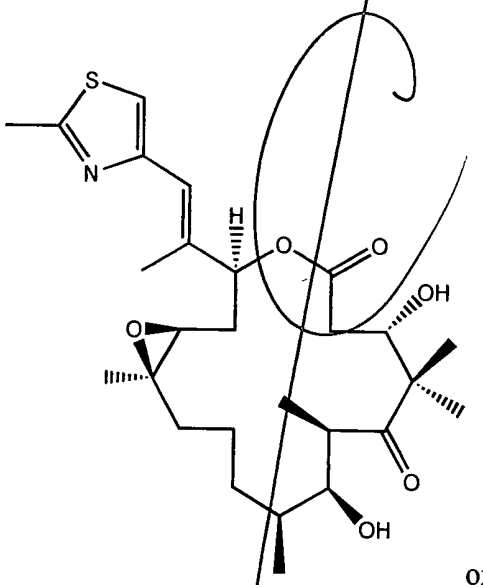
; or



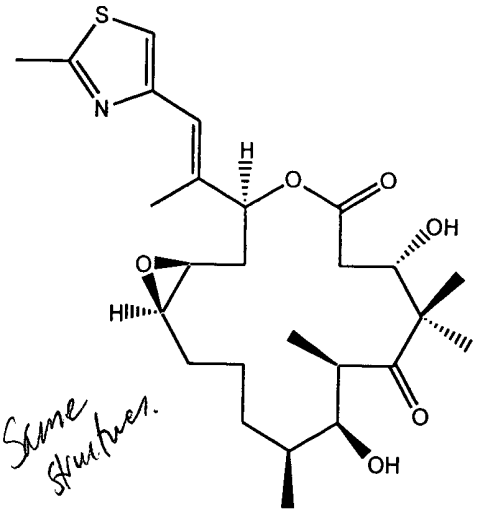
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally

substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

131. A pharmaceutical composition comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:

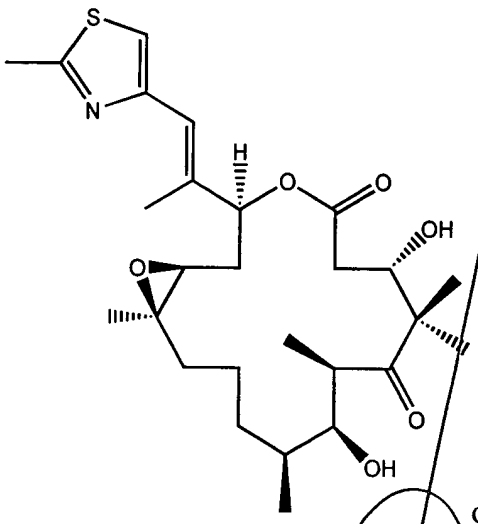


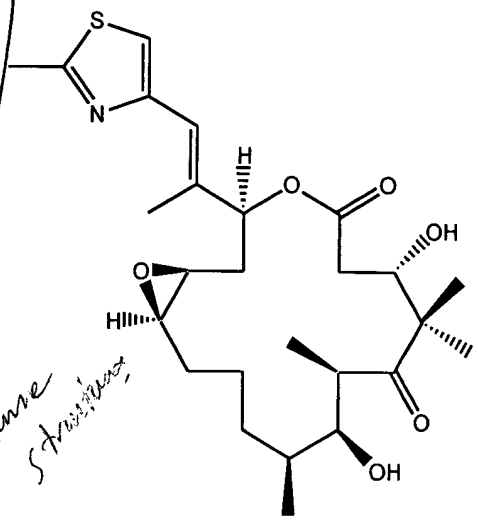
or



; and wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

132. A pharmaceutical composition comprising a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier, wherein the compound has the structure:

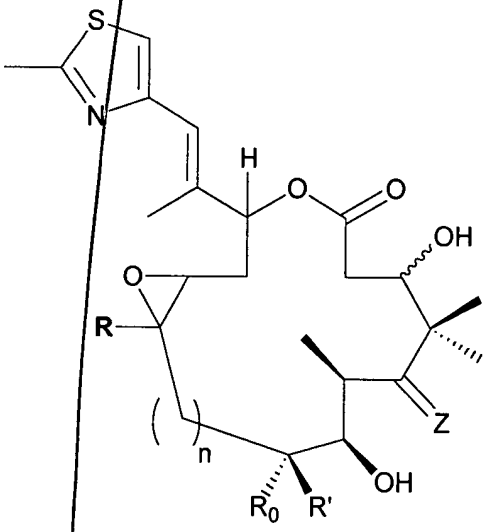




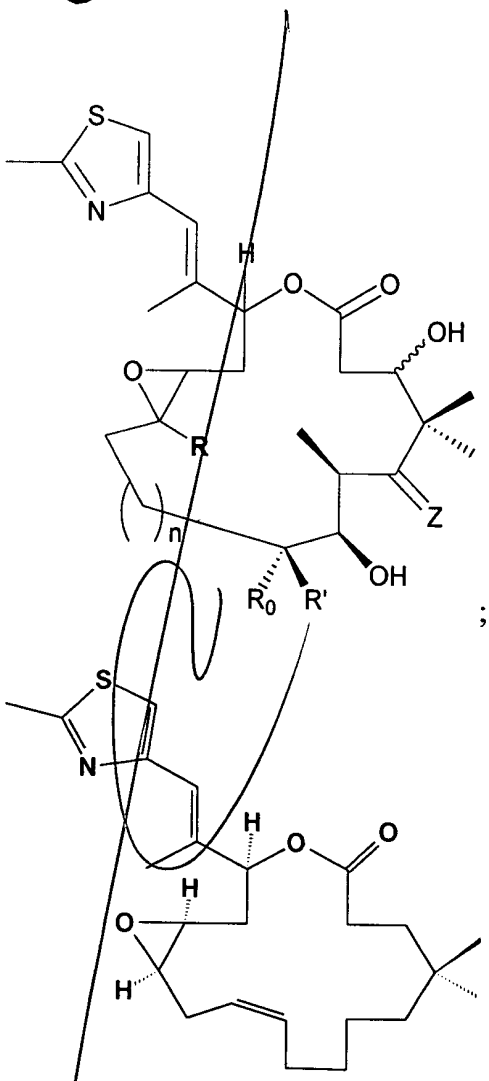
or ; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

133. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



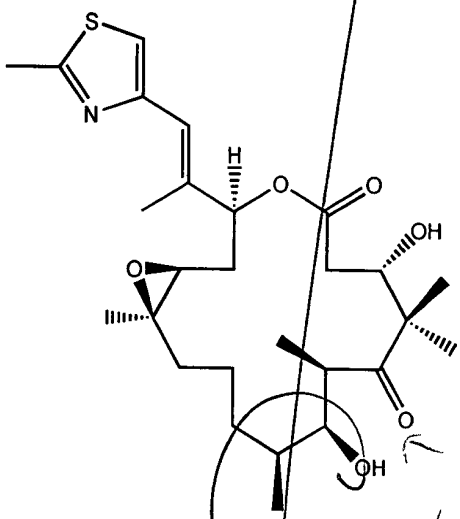
;



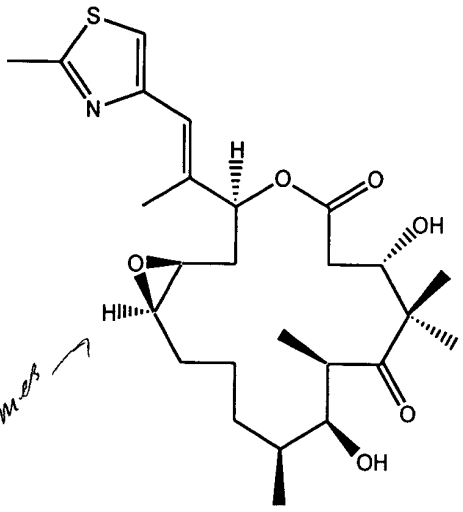
; or

wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

134. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound having the structure:



or

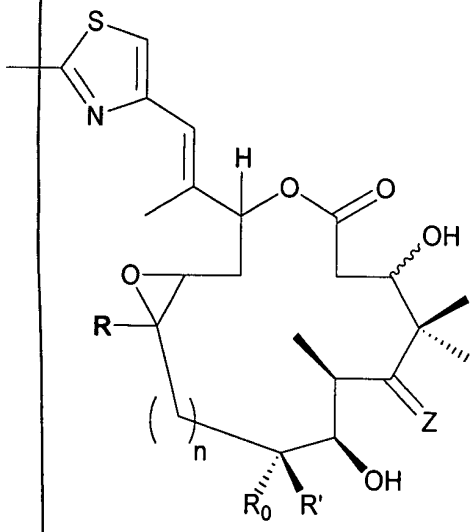


; and

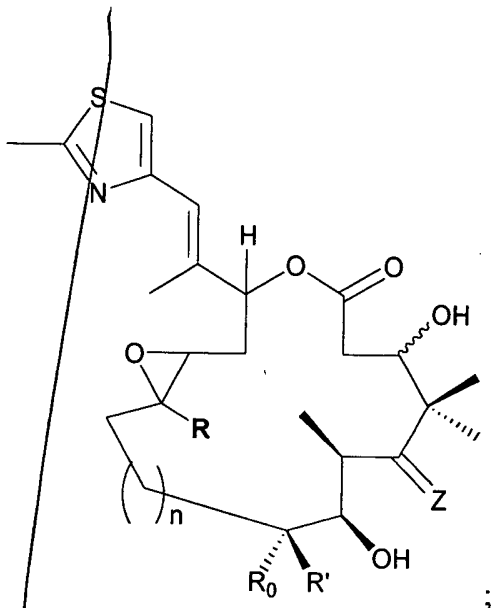
wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

135. The method of claim 71, wherein the step of administering comprises:

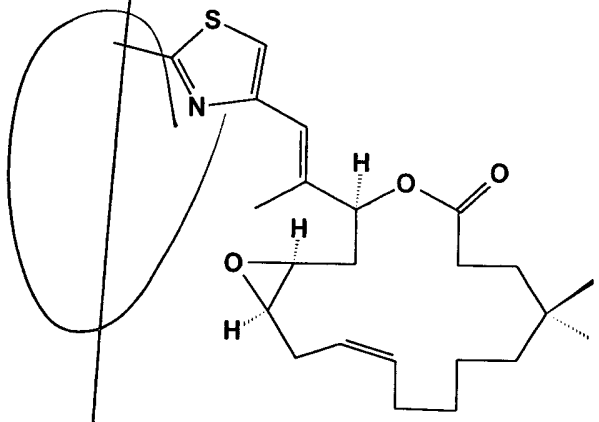
administering to the subject multiple times a therapeutically effective amount of a compound having the structure:



;



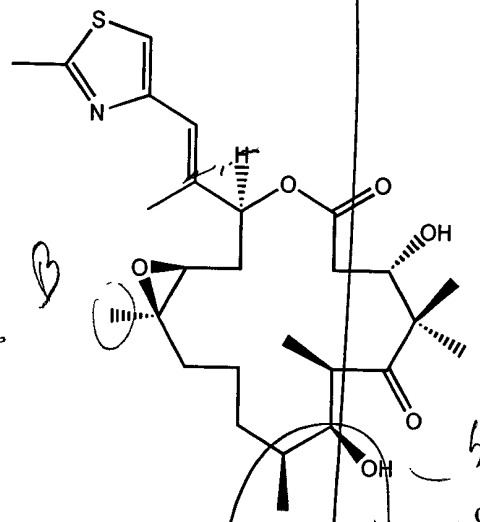
; or



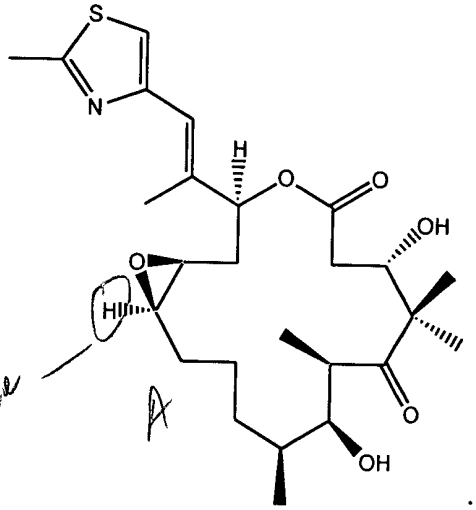
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

136. The method of claim 134, wherein the step of administering comprises:

administering to the subject multiple times a therapeutically effective amount of a compound having the structure:



or

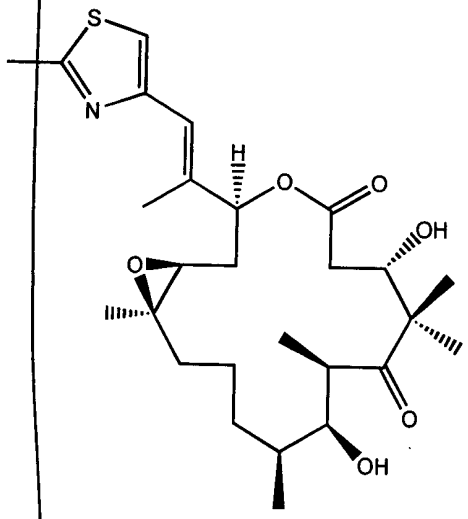


; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

137. The method of claim 124, wherein the step of administering comprises:

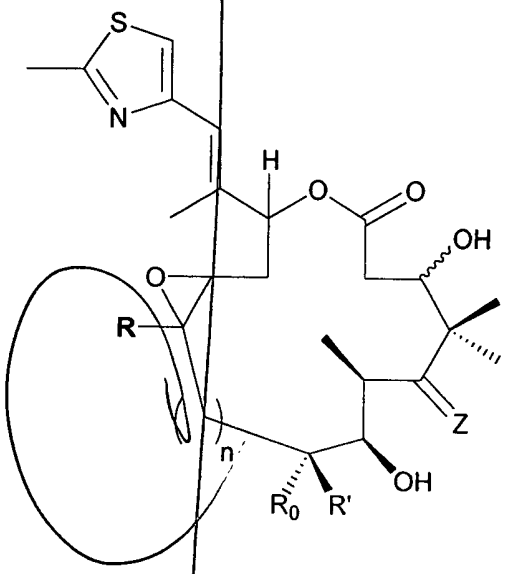
administering to the subject multiple times a therapeutically effective amount of a compound having the structure:



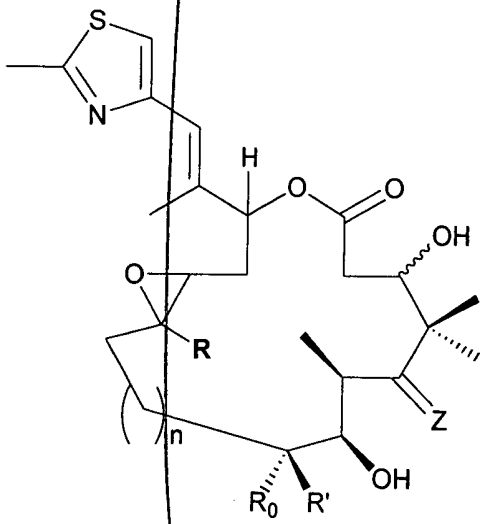
wherein the therapeutically effective amount comprises an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

138. The method of claim 71, wherein the step of administering comprises:

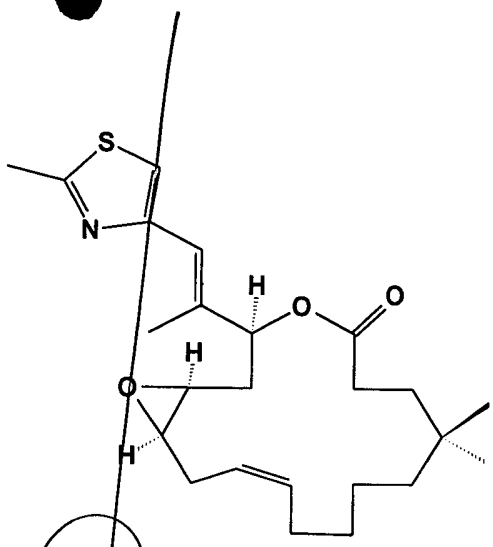
administering to the subject in multiple doses a therapeutically effective amount of a compound having the structure:



;



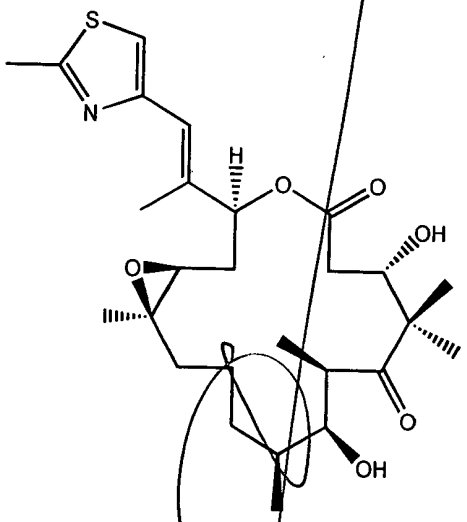
; or



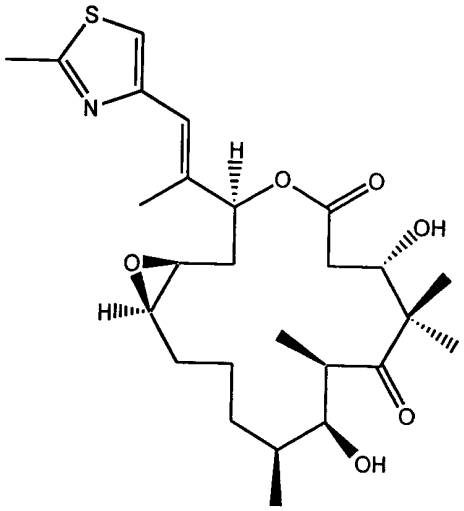
wherein R, R_0, and R′ are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldehyde, linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2, N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N\text{-}NR_4R_5$, wherein R_3, R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3; and wherein the therapeutically effective amount of the compound is amount sufficient to deliver about 0.001 mg to about 10 mg compound per kg body weight.

139. The method of claim 134, wherein the step of administering comprises:

administering to the subject in multiple doses a therapeutically effective amount of a compound having the structure:



or

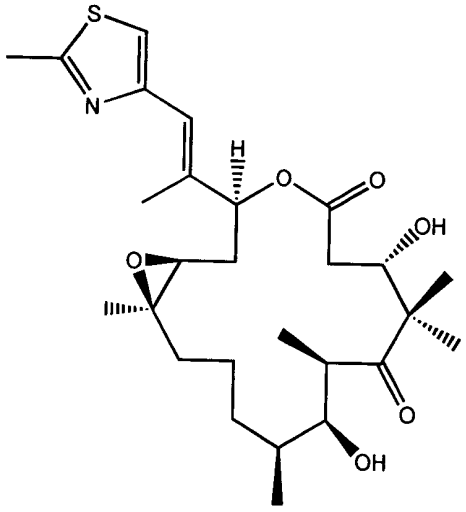


; and

wherein the therapeutically effective amount of the compound is an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

140. The method of claim 124, wherein the step of administering comprises:

administering to the subject in multiple doses a therapeutically effective amount of a compound having the structure:



wherein the therapeutically effective amount comprises an amount sufficient to deliver about 0.001 mg to about 40 mg compound per kg body weight.

141. The composition of claim 30, further comprising at least one additional cytotoxic agent.

142 The composition of claim 139, wherein said at least one additional cytotoxic agent is an anti-cancer agent.

143. The composition of claim 140, wherein the anti-cancer agent is selected from the group consisting of adriamycin, vinblastin, and paclitaxel.